Minutes of Meeting

Alabama Medicaid Agency
Pharmacy and Therapeutics Committee

February 22, 2006

Attendees: Dr. A. Z. Holloway, Chair; Ms. Sheri Lynn Boston, Dr. Lucy Culpepper, Mr. Timothy Cummins, Dr. Denise DeBellis, Dr. Nan Ferris, Dr. Richard Freeman, Dr. W. Thomas Geary, Ms. Kelli Littlejohn, Mr. Ben Main, Dr. Mary McIntyre, Dr. Lucian Newman, III, Dr. Kalindi Raval and Mr. Dane Yarbrough

Absent: none

1. OPENING REMARKS

Prior to the official start of the meeting, Ms. Littlejohn made some housekeeping announcements. Chairman Holloway called the Pharmacy and Therapeutics (P&T) Committee Meeting to order at 9:07 a.m.

2. APPROVAL OF MINUTES

Chairman Holloway asked if there were any corrections to the minutes from the December 14, 2005 P&T Committee Meeting. Dr. Geary asked that the minutes be corrected to read that he "has seen horrible side effects" rather than "has had horrible outcomes with all of the cholinesterase inhibitors"(page 4, paragraph 7, sentence 5). There were no other changes or corrections to the minutes. A motion was made and seconded to approve the amended minutes.

3. PHARMACY PROGRAM UPDATE

Ms. Littlejohn gave the pharmacy program update. On January 1, 2006, in accordance with the Centers for Medicaid and Medicare (CMS) guidance, Alabama Medicaid no longer covers any drug used for sexual or erectile dysfunction. Alabama Medicaid does have special allowances for the phosphodiesterase inhibitors used for recipients with pulmonary hypertension. Also on January 1, Medicare Part D became effective. The dually eligible population moved from Medicaid pharmacy coverage to Medicare Part D pharmacy coverage. In response to the Janaury 1 change, Medicaid gave financial advancements to pharmacies to aid with Medicare Part D. The advancement was based on the December 2005 dually eligible expenditures rounded to 75% for each pharmacy provider. On January 20, 2006, a check for this amount was advanced to the pharmacy providers as an interest free advancement. Long-term care pharmacy providers were asked to sign a promissory note and their advancement will be due back to the Agency on July 31, 2006. For all other providers, the advancement will be retracted on subsequent check writes in March, April and May, in three equal installments. Also on January 20, Relenza® and Tamiflu® were designated preferred status on the Preferred Drug List (PDL) until March 31 in response to the Centers for Disease Control's announcement of this year's flu season and resistance to certain products. Relenza® and Tamiflu® will require prior authorization (PA) beginning April 1, 2006.

On February 1, quarterly updates to the PDL were made. The quarterly updates were done on February 1 instead of January 1 because of the Medicare Part D implementation. Also, as of February 1, generic omeprazole will require PA. Ms. Littlejohn noted that there are several preferred products on the PDL within this class.

The agency extended the Synagis® season from March 15 to March 31. All other criteria will remain the same and the number of doses approved for the season will remain at five.

The next quarterly update to the PDL will be April 3, 2006. At this time, generic alprazolam will be added to the drug file. This change is in response to a request from the P&T Committee and approval by the Commissioner.

Dr. Ferris introduced Denise DeBellis, Pharm.D., and Kalindi Raval, Pharm.D., clinical pharmacists who had assisted with the preparation of the clinical packets and would be assisting with the presentations of the pharmacotherapy re-reviews. Mr. Timothy Cummins, Executive Director of Clinical Pharmacy Services, was also introduced to the P&T Committee.

Ms. Littlejohn noted that Health Information Designs (HID) worked with a statistician to determine whether there was a statistically significant difference between medical costs before and after implementation of the PDL. Mark Carpenter, Ph.D., Director of Statistics from the Department of Mathematics and Statistics at Auburn University, prepared the analysis. Charts noting the medical costs per month by therapeutic class and the statistical significance of any changes were distributed to the P&T Committee Members. The charts were similar to those presented at the October 12, 2005 meeting; however, data regarding the dually eligible members was excluded. Ms. Littlejohn noted that there was a significant reduction in medical costs for several therapeutic classes ($p < 0.05$). Chairman Holloway asked that Dr. Carpenter be invited to attend and discuss his analyses at the next P&T Committee Meeting.

4. ORAL PRESENTATIONS BY MANUFACTURERS/MANUFACTURERS' REPRESENTATIVES

Five-minute verbal presentations were made on behalf of some pharmaceutical manufacturers. The drugs and corresponding manufacturers are listed below with the appropriate therapeutic class. There were a total of 10 manufacturers' presentations at the meeting.

5. PHARMACOTHERAPY REVIEWS-RE-REVIEWS (Refer to the web for full text reviews):

The pharmacotherapy reviews began at approximately 9:15 a.m.

Antiarrhythmic Agents AHFS 240404

Manufacturer comments on behalf of these products:

None

Dr. Raval began her presentation by noting that the antiarrhythmic agents were previously reviewed in March of 2004. Since that review, no new antiarrhythmic agents have been added to the market. Most of these products are available generically, with the exception of dofetilide and moricizine. Dr. Raval noted that with this clinical packet, Table 1 includes a column that indicates what generic and brand products are currently on the Alabama Medicaid Preferred Drug List (PDL). In the current PDL Reference Tool, quinidine gluconate is not listed, but with the next reference tool update, generic quinidine gluconate will be listed.

For each of the common arrhythmias, there are several drugs of choice and alternatives that are available generically. Considerations in choosing antiarrhythmic therapy should be based on presence of cardiovascular disease as well as type of arrhythmia. There have been no significant changes in the pharmacokinetics section and minor changes to the drug interaction sections. The dofetilide boxed warning

was noted, which states that patients initiated or reinitiated on dofetilide should be monitored as inpatients to minimize the risk of induced arrhythmias.

Dr. Raval highlighted the updates to the effectiveness section which included findings from the CAST study that warn of arrhythmogenic potential of class I antiarrhythmic agents and recommend that the selection of certain antiarrhythmic agents (for example, Class I) should be reserved for the suppression and prevention of documented life-threatening ventricular arrhythmias. The AFFIRM trial and the trial by Van Gelder et al found no significant difference in mortality and clinical events between groups treated by rhythm control compared to rate control for atrial fibrillation. There are limited comparative trials for the antiarrhythmic agents.

Therefore, all brand products within the class are comparable to each other and to the generic products and offer no significant clinical advantage over other alternatives in general uses. No brand antiarrhythmic agent was recommended for preferred status and Alabama Medicaid should accept cost proposals from manufacturers of antiarrhythmic agents to determine cost effective products and possibly designate one or more preferred agents.

There were no further discussions on the drugs in this class. Chairman Holloway asked the P&T Committee Members to mark their ballots.

Cardiotonic Agents AHFS 240408
Manufacturer comments on behalf of these products:
None

Dr. Raval noted that the cardiotonic agents were previously reviewed in March of 2004. Since that review, no new cardiotonic agents or new formulations have been added to the market.

Dr. Raval highlighted the 2005 American College of Cardiology and American Heart Association guideline recommendation that digoxin should be used with a diuretic and an angiotensin-converting enzyme (ACE) inhibitor for the treatment of heart failure when possible. In addition, digoxin is one of several drugs of choice for rate control in the treatment of atrial fibrillation or flutter.

There were no significant changes in the pharmacokinetics, drug interaction, or adverse drug event sections. However, pediatric dosing recommendations have been included in this review. Dr. Raval noted that the effectiveness section had been updated.

Therefore, all brand products within the class are comparable to each other and to the generic products and offer no significant clinical advantage over other alternatives in general use. No brand cardiotonic agent was recommended for preferred status and Alabama Medicaid should accept cost proposals from manufacturers of cardiotonic agents to determine cost effective products and possibly designate one or more preferred agents.

There were no further discussions on the drugs in this class. Chairman Holloway asked the P&T Committee Members to mark their ballots.

Nitrates and Nitrites AHFS 241208
Manufacturer comments on behalf of these products:
None

Dr. Raval noted that the nitrate and nitrite agents were previously reviewed in March of 2004. Since that review, no new nitrate or nitrite agents or formulations have been added to the market. Currently, generic products for acute angina attacks and for chronic stable angina are available on the Alabama Medicaid PDL. Amyl nitrite was originally approved to treat angina, but is frequently abused and commonly referred to as "poppers". It is not currently on the Alabama Medicaid PDL. (Note: after the meeting, it was determined that amyl nitrite was a covered agent.)

Dr. Raval noted that there have been no significant changes in the pharmacokinetics, drug interaction, or adverse drug event sections. Dr. Raval highlighted that since nitrates have the same pharmacologic effects, the product selection is based on desired onset and duration of action. Although there is no generic spray formulation, the nitroglycerin spray possesses no known clinical advantage over the sublingual tablets.

Therefore, all brand products within this class reviewed are comparable to each other and to the generics in this class and offer no significant clinical advantage over other alternatives in general use. No brand nitrates or nitrites were recommended for preferred status and Alabama Medicaid should accept cost proposals from manufacturers of nitrates and nitrites to determine cost effective products and possibly designate one or more preferred agents.

There were no further discussions on the drugs in this class. Chairman Holloway asked the P&T Committee Members to mark their ballots.

Bile Acid Sequestrants AHFS 240604
Manufacturer comments on behalf of these products:
None

Dr. Ferris pointed out that the American Hospital Formulary Service (AHFS) has classified the Antilipemic Agents into several categories, including the bile acid sequestrants (BAS), cholesterol absorption inhibitors, fibric acid derivatives, hydroxymethylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors, and miscellaneous antilipemic agents (which include niacin).

The BAS were the first class of Antilipemic Agents to be reviewed. Dr. Ferris noted that cholestyramine is the only BAS that is available generically and on the Alabama Medicaid PDL. The BAS are all indicated as either monotherapy or in combination with an HMG CoA-reductase inhibitor, also called a “statin”, to reduce elevated low-density lipoprotein cholesterol (LDL-C) in primary hypercholesterolemia. Cholestyramine has the additional indication to treat pruritus associated with biliary obstruction.

Dr. Ferris noted that the BAS are not absorbed but form insoluble complexes that are excreted in the feces. Cholestyramine and colestipol may interfere with the absorption of other drugs, which may be minimized by taking other drugs at least 1 hour before or 4-6 hours after cholestyramine or colestipol. Colesevelam does not appear to interfere with the absorption of co-administered drugs but the manufacturer recommends considering monitoring drug levels or effects when administering concomitantly with drugs that have a narrow therapeutic window.

Gastrointestinal side effects are the most frequent adverse events reported with the BAS. The adverse effects of colestipol and cholestyramine are similar. Colesevelam appears to be better tolerated, with fewer GI symptoms; however, there are no head-to-head trials comparing these agents. All of the BAS can be dosed either once or twice a day.

Clinical studies regarding the effectiveness of the BAS were discussed. In a large, placebo-controlled trial, cholestyramine reduced LDL-C by 20% and resulted in a 19% reduction in the combined rate of coronary heart disease death plus nonfatal myocardial infarction (MI) relative to placebo ($P < 0.05$). Other studies demonstrated that the addition of cholestyramine to a statin produced additional benefits. Cholestyramine has been shown to be comparable in efficacy to colestipol with both resulting in decreases in total cholesterol of 10 to 15%. A small increase in triglycerides was observed in some patients. One study reported compliance was better with colestipol; however, cholestyramine was rated as more palatable in another study. Clinical studies have demonstrated that colesevelam was more effective than placebo in decreasing total cholesterol and LDL-C and increasing high-density lipoprotein cholesterol (HDL-C). In combination with a statin, the addition of colesevelam produced greater effects.

In conclusion, the BAS have been shown to have modest efficacy in reducing LDL-C (up to 20%) with slight increases in HDL-C. The BAS appear to be comparable in efficacy; however, there are no head-to-head trials between colesevelam and cholestyramine or colestipol. The BAS may provide an alternative therapy to patients who require modest LDL-C reduction and who are refractory or intolerant to other lipid lowering agents, such as the statins. The BAS may also be useful as adjunctive therapy to statins when the statin alone is insufficient or there are safety issues related to increasing the dose of the statin.

Therefore, all brand products within the class reviewed are comparable to each other and to the generics and over-the-counter (OTC) products in this class and offer no significant clinical advantage over other alternatives in general use.

No brand BAS was recommended for preferred status and Alabama Medicaid should accept cost proposals from manufacturers to determine cost effective products and possibly designate one or more preferred agents.

Chairman Holloway asked if there were any questions or comments. Dr. Newman inquired about the regulations regarding the off-label uses of cholestyramine, for example, post-cholecystectomy diarrhea. Ms. Littlejohn replied that currently the Agency does not support off-label use; however, in Alabama a diagnosis is not tied along with a prescription. With the preferred agents, a diagnosis code is not required and the Agency is not able to capture claims for off-label uses.

Chairman Holloway inquired if we were moving into a situation where prescribers would not be able to write prescriptions for off-label uses. Ms. Littlejohn replied that from her understanding that would require movement from the State Board of Pharmacy to require diagnosis on the prescription. Dr. McIntyre remarked that there was no movement from the Agency in this direction.

There were no further discussions on the drugs in this class. Chairman Holloway asked the P&T Committee Members to mark their ballots.

Cholesterol Absorption Inhibitors 240605
Manufacturer comments on behalf of these products:
None

Dr. Ferris noted that at this time ezetimibe is the only agent classified as a cholesterol absorption inhibitor and it is not currently on the Alabama Medicaid PDL. There are no generic or OTC products in this class. Ezetimibe is primarily indicated for the treatment of hypercholesterolemia, either alone or in combination with a statin.

Dr. Ferris mentioned that ezetimibe is extensively metabolized in the small intestine and liver to an active metabolite. The pathway is glucuronide conjugation so ezetimibe has minimal propensity to interact with the cytochrome P450 substrates. Coadministration of ezetimibe with fibric acid derivatives is not recommended because of a potential increased risk of cholelithiasis. The most common side effects are gastrointestinal. The recommended dose of ezetimibe is 10 mg once daily.

Dr. Ferris presented several clinical studies noting that compared to placebo, ezetimibe resulted in a 17% decrease in LDL-C. When ezetimibe was added to a statin, overall, ezetimibe resulted in an additional 12%-21% lowering of LDL-C compared to statin monotherapy. Additional benefit was seen in the total cholesterol, triglycerides and HDL-C. Ezetimibe plus a low dose statin had about the same efficacy as a high dose of a statin alone.

Dr. Ferris concluded that ezetimibe provides only modest reductions in LDL-C, with minor effects on HDL-C and triglycerides. Ezetimibe's primary role is in combination with a statin in patients unable to achieve or sustain target LDL levels on a statin alone or to reduce the dose of a statin required to achieve target levels. Additional studies are necessary to determine if the combination of ezetimibe plus a statin is associated with fewer side effects in comparison with increasing the dose of the statin. No trial has yet evaluated clinical outcomes with ezetimibe alone or in combination therapy. Compared to other lipid-lowering adjunctive therapies within alternative drug classes, ezetimibe offers a level of LDL-C reduction, which appears to be comparable, although head-to-head comparisons are currently lacking.

Therefore, all brand products within the class appear to offer no significant clinical advantage over other alternatives in general use. No brand cholesterol absorption inhibitor was recommended for preferred status and Alabama Medicaid should accept cost proposals from manufacturers to determine most cost effective products and possibly designate one or more preferred brands.

There were no further discussions on the drugs in this class. Chairman Holloway asked the P&T Committee Members to mark their ballots.

Fibric Acid Derivatives AHFS 240606
Manufacturer comments on behalf of these products:
Tricor® (fenofibrate) – Abbott Laboratories
Triglide® (fenofibrate) – First Horizon

Prior to the manufacturers' oral presentations, Ms. Littlejohn explained the lighting and timing system for the manufacturers' presentations.

Dr. DeBellis presented this therapeutic class and began her presentation by noting that the fibric acid derivatives were previously reviewed in December 2003. Dr. DeBellis mentioned that gemfibrozil was available generically and was on the Alabama Medicaid PDL. There are several formulations of fenofibrate, and recently, a generic micronized fenofibrate formulation was FDA-approved.

Dr. DeBellis noted that the fibric acid derivatives are primarily used for the treatment of hypertriglyceridemia, but may also be used to treat primary hypercholesterolemia or mixed dyslipidemias. Gemfibrozil and fenofibrate demonstrated comparable effects on lipid levels and efficacy. Only one trial directly compared the efficacy of gemfibrozil and fenofibrate; however, this trial was limited by the fact that the maximum dose of fenofibrate was not compared to the recommended dose of gemfibrozil. Both gemfibrozil and fenofibrate are supported by clinical trials that show reduction in patient-oriented outcomes (cardiovascular morbidity and/or mortality).

The pharmacokinetic parameters and safety of these agents were noted to be comparable. The only minor difference amongst the fenofibrate formulations is that the newer formulations (the micronized and nanocrystals), are preferentially taken with food, which in turn increases bioavailability, by roughly 33%. Gemfibrozil may possess a greater potential to increase statin serum levels when both agents are administered concurrently. All of the fibric acid derivatives are fairly well tolerated and no clear differences exist in side effects.

Therefore, all brand products within the class reviewed are comparable to each other and offer no significant clinical advantage over other alternatives in general use. No brand fibric acid derivative was recommended for preferred status and Alabama Medicaid should accept cost proposals from manufacturers to determine cost effective products and possibly designate one or more preferred agents.

There were no further discussions on the drugs in this class. Chairman Holloway asked the P&T Committee Members to mark their ballots.

HMG-CoA Reductase Inhibitors AHFS 240608
Manufacturer comments on behalf of these products:
Altoprev® (extended-release lovastatin) – First Horizon
Crestor® (rosuvastatin) – AstraZeneca
Lipitor® (atorvastatin) – Pfizer

Dr. DeBellis noted that the HMG-CoA Reductase Inhibitors (statins) were previously reviewed in December 2003. She identified lovastatin as the only statin that is available generically at this time. Statins that are currently on the Alabama Medicaid PDL include generic lovastatin, Lescol®, Lescol XL®, Altoprev®, Crestor® and Zocor® .

Dr. DeBellis mentioned that the statins are considered first-line agents for treating hyperlipidemia due to their ability to favorably impact multiple lipid parameters including LDL-C, HDL, and triglycerides. She pointed out three main issues that require consideration when selecting a statin for preferred drug status and they include safety, LDL-C lowering capacity and patient outcomes data. Dr. Debellis noted that clinically important drug interactions exist for the statins although there are minor differences between the drugs when

evaluating their use in the general population. In addition, no clear differences exist between the statins in the rates of adverse effects.

Dr. DeBellis highlighted recent pivotal trials that focused on intensive lipid lowering since the most recent guidelines emphasize aggressive lipid lowering. Within the statin class, the agents with the most potent LDL-C lowering capacity include atorvastatin, rosuvastatin and simvastatin. However, all statins exert a dose-dependent cholesterol lowering capacity. Dr. DeBellis noted that each statin, with the exception of rosuvastatin, has demonstrated a reduction in cardiovascular morbidity and mortality.

MedMetrics recommended that Alabama Medicaid work with the manufacturers on cost proposals so that at least one statin (atorvastatin, lovastatin, pravastatin or simvastatin) that has demonstrated positive morbidity and mortality outcomes was selected as a preferred agent. MedMetrics also recommended that Alabama Medicaid work with manufacturers of atorvastatin, rosuvastatin and simvastatin on cost proposals so that at least one high-potency HMG-CoA reductase inhibitor is selected as a preferred agent. The final recommendation was that Alabama Medicaid should accept proposals from the remaining manufacturers to determine cost effective products and possibly designate additional preferred agents.

Chairman Holloway asked if there were any questions or comments. Dr. Culpepper inquired if there was a limit on the number of statins that could be added to the Alabama Medicaid PDL. Ms. Littlejohn replied there was no limit, and they encouraged the manufacturers to work with them on cost proposals to have as many brands as possible on the PDL.

Dr. Newman inquired when pravastatin would be available generically. Dr. DeBellis replied that her information sources indicated mid 2006.

Dr. Newman also inquired how the current agents on the PDL were determined, as there were so many agents on the PDL, except for atorvastatin and pravastatin. Ms. Littlejohn commented that the agents currently on the PDL were based on recommendations from a previous P&T meeting. After clinical considerations and P&T recommendations were taken into account, additional agents were added based on cost effectiveness. Discussion followed on the history of current antilipemic preferred agents.

There were no further discussions on the drugs in this class. Chairman Holloway asked the P&T Committee Members to mark their ballots.

HMG-CoA Reductase Inhibitors – Combination Products AHFS 240608
Manufacturer comments on behalf of these products:
Caduet® (atorvastatin/amlodipine) – Pfizer
Vytorin® (simvastatin/ezetimibe) – Merck/Schering-Plough

Dr. DeBellis began her presentation by noting that the HMG-CoA Reductase combination products are not regularly used as first-line agents, but are often used when monotherapy proves insufficient in reaching goals. The combination products demonstrate the same clinically important drug interactions and adverse effects as their individual components. There are minor differences between the drugs when evaluating their use in the general population and these differences are not clinically significant.

Dr. DeBellis mentioned there is an abundance of data with the statin products found in these combinations; however, there are very few studies available for the combination products as a whole. She mentioned that all of the studies focus on surrogate markers as primary and secondary endpoints (such as lipid parameters or blood pressure lowering), as opposed to patient-related outcomes (morbidity and mortality). Additionally, the majority of the clinical trials compared the combination product to an individual component or placebo. Notably, there were no observed differences in outcomes with the combination products as compared to co-administration of their individual components. The combination products demonstrated no clinical advantage over the individual components when co-administered.

Therefore, all brand products within the class reviewed are comparable to each other and offer no significant clinical advantage over other alternatives in general use. No brand HMG-CoA reductase inhibitor combination product was recommended for preferred status and Alabama Medicaid should accept cost proposals from manufacturers to determine cost effective products and possibly designate one or more preferred agents

Chairman Holloway asked if there were any questions or comments. Dr. Newman did not feel that it was possible to compare these products because they are so different. He commented that by adding an aspirin or a Zetia® or an antihypertensive to a statin, we would assume that the results would be better, but the end points would be different. He expressed concerns about compliance and felt it would be beneficial to know how we were doing with regards to compliance while making decisions on statins and antihypertensive agents. He felt that the combination agents will be used with increasing frequency. He suspected that BlueCross and BlueShield formulary might be offering these agents in the near future. His understanding was that in Europe it was almost standard practice, and inquired if this was true. Dr. DeBellis commented that she did not know if this was standard practice in Europe. She stated that the agents included within this review were based upon the AHFS classification system. She also commented that there are no large trials that looked at adherence rates while taking the individual components versus the combination product. Dr. Newman expressed interest in obtaining more information on how we were doing with regards to optimal control of hypertension and lipids with standard agents or monotherapy. He noted that when you add multiple medicines, the compliance rate for all of the medications goes down. His opinion is that the combination products will be used with increasing frequency in the future and questioned where we should position these medications for this population.

Dr. DeBellis noted that these products are not considered first-line because they are available in a fixed-dose combination. She mentioned that if you were initiating therapy, you would not start with a combination product, but would start with the individual components and adjust therapy accordingly.

Dr. Freeman felt that of all the combination products discussed, only Advicor®, with the Niaspan® component, addresses Lp (a). He was not aware of any other medication like the extended-release niacin or brand Niaspan® that would increase HDL, lower LDL, and decrease triglycerides, and at the same time lower Lp (a). He felt Advicor® was a valuable combination, particularly when talking about compliance. He felt that the statin dose should be reduced to the lowest dose to get the desired effect. Ms. Littlejohn noted that the niacin products would be the next therapeutic class reviewed.

Dr. McIntyre mentioned that they had previously conducted a review on compliance and adherence. She noted that the previous review was comprehensive and addressed patient compliance as a general issue, as there are limited studies looking at specific drugs and clinical outcomes. The review included comparisons

of various dosing regimens, such as once daily, twice daily and four times daily. It would be advantageous to revisit this issue again and bring this review before the P&T Committee during the next meeting.

Mr. Main expressed concerns about the four-brand limit and that patients may not take their medications if they exceed the four-brand limit. Dr. Ferris noted that within these therapeutic classes there are generic alternatives for the components of the combination products, so that instead of using two brand products, generics may be considered. She also noted that the recommendations should be evaluated for use within the general population rather than specific or niche populations. She expressed concern that once an agent was added onto the PDL, it almost becomes first-line because there would be unlimited access to the product.

Chairman Holloway asked Dr. Geary if combination products were used as first-line or second-line in the nursing home. Dr. Geary commented that they generally use generics in the nursing homes. Dr. Geary inquired if anyone knew how these drugs were tiered in any of the 42 Medicare Part D Preferred Drug Programs (PDP). Ms. Littlejohn reported that there were limited PDPs that automatically enrolled the dually eligible recipients. She commented that the Medicare Part D PDP was a federally tiered program, and must have an appeals process, minimum of 2 drugs in each drug class, and a 30-day transition period. Other than those requirements, a major difference is that Medicaid is required to cover all agents (even though they may PA some agents), whereby the PDP are not required to cover all agents. She said that she was not able to address a specific PDP, but was aware that they may have a tiered structure, prior usage requirements and maximum units. Mr. Yarbrough mentioned that the PDPs are "a mixed bag". There is some movement for some of the combination products to be placed in tier 1, but most of the combination products are at a tier 2 or 3 level. Dr. Geary noted that CMS has suggested that the total number of pills be reduced. A combination product would be counted as one pill. He also commented that his population was in a controlled environment with specific medication administration schedules.

Mr. Main stated that he would encourage the manufacturers to work with Medicaid.

There were no further discussions on the drugs in this class. Chairman Holloway asked the P&T Committee Members to mark their ballots.

Chairman Holloway commented about the use of the phrase "for general use" within the Medicaid population. Dr. McIntyre clarified that when we evaluate recommendations for PDL inclusion, we are evaluating their use for the general Medicaid population.

Miscellaneous Antilipemic Agents AHFS 240692
Manufacturer comments on behalf of these products:
Niaspan® (extended-release niacin) – KOS Pharmaceuticals

Ms. Littlejohn reminded the manufacturers that they are not allowed to bring cost into their presentations.

Dr. DeBellis noted that the miscellaneous Antilipemic Agents, which include niacin, were previously reviewed in December 2003. Niacin is available in many different OTC and prescription formulations.

Dr. DeBellis mentioned that niacin is not as widely used as the statins, but is a treatment option for combined dyslipidemias. In comparison to the statins or fibric acid derivatives, niacin is the most effective

agent for increasing HDL levels. The lipid lowering capacities of the niacin products are comparable. The same is true for drug interactions. However, there are significant differences in adverse effects and safety between the various niacin products. It was pointed out that the risk of liver toxicity is significantly greater with some sustained-release formulations of niacin.

Dr. DeBellis mentioned that the FDA classifies all OTC niacin formulations as "dietary supplements." In addition, the American Heart Association (AHA) states that OTC niacin must not be used as a substitute for prescription niacin because these agents are not regulated in the same manner as prescription niacin. Furthermore, the AHA states that OTC sustained-release niacin should not be used for cholesterol lowering because of potentially very serious side effects including hepatotoxicity.

Dr. DeBellis concluded that the information provided narrows the choices to two products, prescription immediate-release or extended-release niacin. The prescription immediate-release and extended-release niacin products are comparable to each other but do appear to offer clinical advantages over OTC products in this class.

MedMetrics recommended prescription niacin for preferred status and that Alabama Medicaid should negotiate with manufacturers of prescription niacin products and possibly designate at least one product for preferred status.

Chairman Holloway asked if there were any questions or comments. Dr. Freeman made a motion, which was seconded by Mr. Yarbrough, to amend the recommendation to place Niaspan® on the PDL in preferred status.

There were no further discussions on the drugs in this class. Chairman Holloway asked the P&T Committee Members to mark their ballots.

Platelet-Aggregation Inhibitors AHFS 920000, Aspirin AHFS 280804 and Dipyridamole AHFS 241292-Single Entity

Manufacturer comments on behalf of these products:

Plavix®(clopidogrel)-sanofi aventis

Dr. Ferris noted that the platelet-aggregation inhibitors were previously reviewed in July of 2003. At that time, no brand was recommended for preferred drug status. Aspirin, cilostazol, dipyridamole and ticlopidine are all available generically and are currently on the PDL. Clopidogrel is currently not on the PDL, but may be obtained through medical justification.

Dr. Ferris presented an overview of the current treatment guidelines for the most common conditions for which the platelet-aggregation inhibitors are prescribed. She noted that these guidelines are evidence-based and resulted from detailed analyses of pivotal trials with the platelet-aggregation inhibitors. Aspirin was the most widely studied antiplatelet agent. Aspirin and clopidogrel are the antiplatelet agents mentioned most frequently in these guidelines. The presentation of the treatment guidelines included the following conditions: acute ischemic stroke, noncardioembolic transient ischemic attack (TIA) or stroke, non-ST-elevation (NSTE) acute coronary syndrome (ACS), post myocardial infarction (MI) and post ACS, chronic stable coronary artery disease, ST-elevation MI, coronary artery bypass grafting, percutaneous coronary intervention, and peripheral arterial occlusive disease. Key pivotal clinical studies were also discussed.

Dr. Ferris pointed out the FDA-approved indications for these agents. She noted there are no significant differences with regards to drug interactions within the doses used for platelet inhibition. The most common side effects of aspirin are gastrointestinal. The guidelines typically recommended a lower aspirin dose in patients at risk for bleeding. Clopidogrel and ticlopidine have been associated with a higher incidence of diarrhea and rash than aspirin.

Dr. Ferris concluded that the platelet-aggregation inhibitors have been shown to significantly reduce the combined odds of stroke, MI or vascular death. Aspirin has been the most frequently studied antiplatelet inhibitor and is recommended either as a first-line or potential first-line agent in most treatment guidelines for general use. Low dose aspirin (75 to 150 mg daily) was shown to be at least as effective as higher daily doses for long-term use.

The other platelet-aggregation inhibitors are indicated for patients with contraindications or severe intolerance to aspirin or for special circumstances. The platelet-aggregation inhibitors that are currently not on the PDL can be obtained through medical justification. Therefore, all brand products within this class reviewed are comparable to each other and to the generics and OTC products in that class and offer no significant clinical advantage over other alternatives in general use. No brand single entity platelet-aggregation inhibitor was recommended for preferred status and Alabama Medicaid should accept cost proposals from manufacturers to determine cost effective products and possibly designate one or more preferred agents.

Chairman Holloway asked if there were any questions or comments. Ms. Boston inquired about the PA process. Dr. McIntyre mentioned that they were currently evaluating the criteria for the platelet-aggregation inhibitors, taking into consideration the current treatment guidelines (e.g., ACS, NSTEMI), the rating of the evidence, and the availability of alternative medications and generics. For some indications, prior usage of alternative medications will not be required. Dr. Culpepper inquired if physicians would still need prior approval for those indications. Dr. McIntyre replied that prior approval would still be needed because the prior approval process is the mechanism to prevent these agents from becoming first-line.

Ms. Littlejohn mentioned that although Alabama does not have a diagnosis tied to a prescription, they have implemented an electronic PA system. The electronic PA system will give an automatic PA if the patient had an ICD-9 code within his/her medical record (within the past 365 days) that was consistent with first-line therapy. If the criteria was met, a manual PA would not be required.

Chairperson Holloway inquired what would happen when a patient was discharged from the hospital with a diagnosis of MI. Dr. McIntyre explained that with the electronic PA process, the diagnosis would not be in the system, and therefore this information would need to be supplied in the medical justification section. The pharmacist or the physician can supply this information, as ACS is one of the acceptable diagnosis codes.

There were no further discussions on the drugs in this class. Chairman Holloway asked the P&T Committee Members to mark their ballots.

Platelet-Aggregation Inhibitors Combination Products Aggrenox® (Aspirin/Dipyridamole) AHFS 241292

Manufacturer comments on behalf of these products:
Aggrenox®(aspirin/extended-release dipyridamole)-Boehringer Ingelheim

Dr. Ferris noted that aspirin and dipyridamole (Aggrenox®) are the only platelet-aggregation inhibitors commercially available as a combination product. There are no platelet-aggregation inhibitor combination products on the Alabama Medicaid PDL.

As discussed in the treatment guidelines for the single entity platelet-aggregation inhibitors, the use of aspirin and dipyridamole are mentioned in the guidelines for the management of stroke. The recommendations by the American College of Chest Physicians (ACCP) and the AHA/American Stroke Association Council on Stroke are similar. For patients with noncardioembolic ischemic stroke or TIA, both groups recommend an antiplatelet agent, and consider initial therapy with aspirin, the combination of aspirin and extended-release dipyridamole or clopidogrel as acceptable options. Compared to aspirin alone, the combination of aspirin and extended-release dipyridamole is safe and suggested instead of aspirin alone (Grade 2A).

Aspirin/extended-release dipyridamole is indicated to reduce the risk of stroke in patients who have had transient ischemia of the brain or complete ischemic stroke due to thrombosis. The pharmacokinetics, drug interactions and adverse drug events are not significantly different than those of the individual components of aspirin and dipyridamole. Aspirin/extended-release dipyridamole is dosed twice daily. The components in this product are aspirin 25 mg and extended-release dipyridamole 200 mg, which are not commercially available, and are not interchangeable with the commercial formulations.

In a post-hoc analysis using data from the European Stroke Prevention Study 2 (ESPS-2), aspirin plus extended-release dipyridamole compared to placebo was more effective in reducing the risk of stroke, with a relative risk reduction of 23%. The difference in efficacy increased in higher risk patients. Results from a large meta-analysis of dipyridamole with or without aspirin for secondary prevention of stroke or TIA were also presented. It was noted that two forms of dipyridamole, the immediate-release and a modified-release formulation, were used in studies. The dosages of aspirin ranged from 50 to 1300 mg. Dipyridamole with and without aspirin reduced stroke recurrence in patients with previous ischemic cerebrovascular disease. Dipyridamole with aspirin reduced the composite of nonfatal stroke, nonfatal myocardial infarction, and vascular death when compared with aspirin alone. This meta-analysis included the results from the European Stroke Prevention Study (ESPS-1), where the combination of aspirin plus dipyridamole (225 mg dipyridamole and 975 mg aspirin per day) was compared to placebo. As noted from the Antithrombotic Trialists' Collaboration in the single entity review, the addition of dipyridamole to aspirin produced no significant further reduction in vascular events compared with aspirin alone.

There are no studies showing that administration of the combination product resulted in better clinical outcomes than compared to administration of the individual agents. Dr. Ferris concluded that dipyridamole and/or aspirin have been shown to reduce stroke recurrence in patients with previous ischemic cerebrovascular disease. Aspirin and dipyridamole reduced the composite of nonfatal stroke, nonfatal MI and vascular death as compared with aspirin alone. Aspirin and dipyridamole are available generically; however, the fixed dose combination product contains strengths of aspirin and dipyridamole that are not commercially available. There are no studies that have shown that the combination product produces better clinical outcomes than administration of the individual ingredients.

Therefore, all brand products within the class reviewed are comparable to each other and to the generics and OTC products in that class and offer no significant clinical advantage over other alternatives in general use. No brand platelet-aggregation inhibitor combination product was recommended for preferred status and Alabama Medicaid should accept cost proposals from manufacturers to determine cost effective products and possibly designate one or more preferred agents.

Chairman Holloway asked if there were any questions or comments. Dr. Culpepper asked for clarification about the availability and strengths of the individual ingredients in the combination products.

There were no further discussions on the drugs in this class. Chairman Holloway asked the P&T Committee Members to mark their ballots.

6. RESULTS OF THE BALLOTING

Ms. Littlejohn announced the results of voting for each of the therapeutic classes. Results of voting are described in the Appendix of the minutes.

7. NEW BUSINESS

There was no new business.

8. NEXT MEETING DATE

The next P&T Committee Meeting was scheduled for 9:00 a.m. on May 24, 2006. If possible, the meeting will be held in the State Capitol Auditorium.

Chairman Holloway asked for further clarification about who can specify the diagnosis and the PA process. Dr. McIntyre replied that the physician must provide the diagnosis. For some therapeutic classes, such as the platelet-aggregation inhibitors, where it is determined that a non-preferred agent is a first-line therapy for a specific diagnosis, the only criteria for approval may be an appropriate diagnosis. Dr. McIntyre commented that it was not difficult to change the criteria, if providers contact them to add additional diagnosis codes to the criteria. Ms. Littlejohn stated that their contractor (HID) is required to notify the prescriber and the pharmacy whether a PA was approved. In addition, their contractor is required to process the PA and respond to both the pharmacy and prescriber within 24 hours. Currently, 90% of the requests are faxed back to the providers within 8 hours and the average processing time is less than 4 hours. The Agency has academic detailers that visit physicians as well as pharmacies and who can address any issues with the pharmacy supervisors.

9. ADJOURN

The meeting was adjourned at 12:00 p.m.

Appendix

RESULTS OF THE BALLOTING
Alabama Medicaid Agency
Pharmacy and Therapeutics Committee
February 22, 2006

A. The P&T Committee voted unanimously to approve the recommendation that no brand antiarrhythmic agent is recommended for preferred drug status. Alabama Medicaid should accept cost proposals from manufacturers to determine cost effective products and possibly designate one or more preferred agents.

Medical Director	[X]	Approve	[ ]	Approve as amended	[ ]	Disapprove	[ ] No action
Deputy Commissioner	[X]	Approve	[ ]	Approve as amended	[ ]	Disapprove	[ ] No action
Commissioner	[X]	Approve	[ ]	Approve as amended	[ ]	Disapprove	[ ] No action

B. The P&T Committee voted unanimously to approve the recommendation that no brand cardiotonic agent is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine cost effective products and possibly designate one or more preferred agents.

Medical Director	[X]	Approve	[ ]	Approve as amended	[ ]	Disapprove	[ ] No action
Deputy Commissioner	[X]	Approve	[ ]	Approve as amended	[ ]	Disapprove	[ ] No action
Commissioner	[X]	Approve	[ ]	Approve as amended	[ ]	Disapprove	[ ] No action

C. The P&T Committee voted unanimously to approve the recommendation that no brand nitrates or nitrites are recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine cost effective products and possibly designate one or more preferred brands.

Medical Director — [X] Approve [ ] Approve as amended [ ] Disapprove [ ] No action

Deputy Commissioner — [X] Approve [ ] Approve as amended [ ] Disapprove [ ] No action

Commissioner — [X] Approve [ ] Approve as amended [ ] Disapprove [ ] No action

D. The P&T Committee voted unanimously to approve the recommendation that no brand bile acid sequestrant is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine cost effective products and possibly designate one or more preferred brands.

Medical Director — [X] Approve [ ] Approve as amended [ ] Disapprove [ ] No action

Deputy Commissioner — [X] Approve [ ] Approve as amended [ ] Disapprove [ ] No action

Commissioner — [X] Approve [ ] Approve as amended [ ] Disapprove [ ] No action

E. The P&T Committee voted unanimously to approve the recommendation that no brand cholesterol absorption inhibitor is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine cost effective products and possibly designate one or more preferred brands.

Medical Director — [X] Approve [ ] Approve as amended [ ] Disapprove [ ] No action

Deputy Commissioner — [X] Approve [ ] Approve as amended [ ] Disapprove [ ] No action

Commissioner — [X] Approve [ ] Approve as amended [ ] Disapprove [ ] No action

F. The P&T Committee voted unanimously to approve the recommendation that no brand fibric acid derivative is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine cost effective products and possibly designate one or more preferred brands.

Medical Director	[X]	Approve	[ ]	Approve as amended	[ ]	Disapprove	[ ] No action
Deputy Commissioner	[X]	Approve	[ ]	Approve as amended	[ ]	Disapprove	[ ] No action
Commissioner	[X]	Approve	[ ]	Approve as amended	[ ]	Disapprove	[ ] No action

G. The P&T Committee voted unanimously to approve the recommendation that Alabama Medicaid should work with the manufacturers on cost proposals so that at least one HMG-CoA reductase inhibitor (atorvastatin, lovastatin, pravastatin or simvastatin) that has demonstrated positive morbidity and mortality outcomes is selected as a preferred agent.

The P&T Committee voted unanimously to approve the recommendation that Alabama Medicaid should also work with manufacturers of atorvastatin, rosuvastatin and simvastatin on cost proposals so that at least one high-potency HMG-CoA reductase inhibitor is selected as a preferred agent.

The P&T Committee voted unanimously to approve the recommendation that Alabama Medicaid should accept proposals from the remaining manufacturers to determine cost effective products and possibly designate additional preferred agents.

Medical Director	[X]	Approve	[ ]	Approve as amended	[ ]	Disapprove	[ ] No action
Deputy Commissioner	[X]	Approve	[ ]	Approve as amended	[ ]	Disapprove	[ ] No action
Commissioner	[X]	Approve	[ ]	Approve as amended	[ ]	Disapprove	[ ] No action

H. The P&T Committee voted unanimously to approve the recommendation that no brand HMG-CoA reductase inhibitor combination product is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine cost effective products and possibly designate one or more preferred brands.

Medical Director	[X]	Approve	[ ]	Approve as amended	[ ]	Disapprove	[ ]	No action
Deputy Commissioner	[X]	Approve	[ ]	Approve as amended	[ ]	Disapprove	[ ]	No action
Commissioner	[X]	Approve	[ ]	Approve as amended	[ ]	Disapprove	[ ]	No action

I. The P&T Committee amended the recommendation that "Prescription niacin is recommended for preferred status" to read "Niaspan® is recommended for preferred status. Alabama Medicaid should negotiate with manufacturers of prescription niacin products and possibly designate at least one product for preferred status." Two members voted to approve as recommended and five members voted to approve as amended.

Medical Director	[X]	Approve	[ ]	Approve as amended	[ ]	Disapprove	[ ]	No action
Deputy Commissioner	[X]	Approve	[ ]	Approve as amended	[ ]	Disapprove	[ ]	No action
Commissioner	[X]	Approve	[ ]	Approve as amended	[ ]	Disapprove	[ ]	No action

J. The P&T Committee voted unanimously to approve the recommendation that no brand single entity platelet-aggregation inhibitor is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine cost effective products and possibly designate one or more preferred brands.

Medical Director	[X]	Approve	[ ]	Approve as amended	[ ]	Disapprove	[ ]	No action
Deputy Commissioner	[X]	Approve	[ ]	Approve as amended	[ ]	Disapprove	[ ]	No action
Commissioner	[X]	Approve	[ ]	Approve as amended	[ ]	Disapprove	[ ]	No action

K. The P&T Committee voted unanimously to approve the recommendation that no brand platelet-aggregation inhibitor combination product is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine cost effective products and possibly designate one or more preferred brands.

Medical Director — [X] Approve [ ] Approve as amended [ ] Disapprove [ ] No action

Deputy Commissioner — [X] Approve [ ] Approve as amended [ ] Disapprove [ ] No action

Commissioner — [X] Approve [ ] Approve as amended [ ] Disapprove [ ] No action

Respectfully submitted,

Nan Ferris

3/15/06

Nan Ferris, Pharm.D. — Date